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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/319,411 10/06/94 NIELSEN

P ISIS1158

EXAMINER

HM12/0827

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ART UNIT

PAPER NUMBER

1655

DATE MAILED:

08/27/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
08/319,411

Applicant(s)

Nielsen et al.

Examiner

Ardin Marschel

Group Art Unit
1655

☒ Responsive to communication(s) filed on Jun 21, 1999

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1, 5, 8-10, 12, 13, 15, 18-20, 22-24, 30-33, 37, and 39-50 is/are pending in the application.

~~On the basis of~~ Claim(s) 2-4, 6, 7, 11, 14, 16, 17, 21, 25-29, 34-36, and 38 have been canceled.
~~are withdrawn from consideration.~~

☒ Claim(s) 39, 41, 44, and 46

is/are allowed.

☒ Claim(s) 1, 5, 8-10, 12, 13, 15, 18-20, 22-24, 30-33, 37, 40, 42, 43, 45, and 47-50 are rejected.

☐ Claim(s) _____

is/are objected to.

☐ Claims _____

are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). (2 sheets)

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

The art unit designated for this application has changed. Applicant(s) are hereby informed that future correspondence should be directed to Art Unit 1655.

Upon reconsideration several rejections have been summarized below which results in withdrawal of the previous indication of allowability of claims.

Applicants' arguments, filed 6/21/99, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 12, 13, 15, 22-24, 30-33, and 47-49 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12, 13, 15, and 22-24 are vague and indefinite due to being incomplete as depending from canceled claims.

Claim 30 is vague and indefinite as to what is meant by the phrase "comprising a plurality of PNA monomers wherein at least one of said PNA monomers has the formula...". Applicants may have intended this claim to indicate that the cited monomers are those from which the PNA conjugate that is claimed are synthesized via polymerization. This is not, however, what the

above phrase states. Alternatively, is the claimed conjugate a mixture of monomers which are not covalently linked into a polymer? If so, a mixture type of wording would clarify what the claimed composition is. This same unclarity is present in claims 47-49. Clarification of what conjugate practice is meant for claims 30 and 47-49 via clearer claim wording is requested. Claims dependent from claim 30 also contain this unclarity due to their dependence.

Claim 30 is additionally vague and indefinite as to what is meant for "1" in the conjugate. "1" is cited in claim 30 on line 36 but without any clear usage in the claimed conjugate. Claims dependent from claim 30 also contain this unclarity due to their dependence. Claims 47-49 also contain this unclarity.

Claim 47, line 37, "R3" lacks antecedent basis due to presumably the lack of correct superscripting. This unclarity is also present in claim 30, 8th line from the end of claim 30.

Claims 18, 19, and 33 are rejected, as discussed below, under 35 U.S.C. § 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claim 18 limits m to be from 1 to about 200 which seems to be broader and therefore not further limiting from claim 37 from which claim 18 depends. Claim 37 limits m to be from 1 to about 50. Claim 19 limits m to be from 1 to about 50 which appears to

be the exact same limitation as the m limitation in claim 37 from which claim 19 depends.

Claim 33 requires R¹³ to be a conjugate which is already a limitation of claim 30 from which claim 33 depends.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1, 8, 12, 13, 15, 18-20, 22-24, 37, 40, 42, 45, and 50 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Thomson et al. (WO 93/12129); recently cited of record.

Thomson et al. describe PNA molecules as depicted on page 5, Formula (I). These PNAs contain a backbone as well as amino and carboxyl ends as required also in instant claims 1 and 37, for

example. These PNAs include an amino linked terminal blocking group depicted as "Q". The genus of species described for this "Q" group is summarized in the bridging paragraph between pages 5 and 6. On page 6, lines 3-8, "Q" is optionally a steriodal moiety having lipophilic character, having a recognition moiety for a cell surface to induce active uptake, or an amine such as given therein on page 6, lines 7-8. Instant claim 1 cites such PNAs with one conjugate moiety specie being a cell receptor binding molecule and another being a crosslinking agent. The genus of "Q" moieties of the reference is deemed to motivate and suggest any specie therein such as a cell surface recognition moiety which is deemed to also be the "cell receptor binding molecule of instant claim 1. Another moiety of the reference that suggests and motivates an instant claim 1 moiety is the amine given in said page 6, lines 7-8, of the reference. This amine results in "Q" being terminated with a primary amine. In the reference the amine is cited as being a ionizable moiety. Another well known practice for primary amines is as crosslinking agents. Although not stated as a crosslinking agent in the reference this characteristic of such an amine is well known to be usable as such in the art which is deemed to motivate and suggest the crosslinking option for a conjugate of claim 1 also. It is also noted that the moiety "J" of the reference is described on page 6, lines 10-13, to include a primary amine

termination which also is deemed to suggest this type of carboxy terminus conjugate of the instant claims as being a crosslinking moiety. The Formula (I) of the reference also depicts the monomeric structures from which these polymers are constructed as given in the synthetic portion of the reference. These monomers are also suggested due to having the same chemical structure as certain species of the monomers of the instant claims.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the instant invention because Thomson et al. suggests and motivates several species therein including a PNA with a cell receptor binding molecule attached on the amino terminus as is also a specie of PNA conjugate that is instantly claimed. Several other terminal conjugate species given in the reference are also made obvious as summarized in the above paragraph.

Claims 1, 8, 12-15, 18-20, 22-24, 37, and 40 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Manoharan et al. (P/N 5,834,607), taken in view of Nielsen et al. [Science 254:1497(1991); already of record].

Manoharan et al. describes the making of amine containing polymeric compounds. These amine containing compounds include PNAs as described in column 6, lines 61-66. The PNAs therein described are generic in nature without being limited as to backbone structure, but citing Nielsen et al. [Science

254:1497(1991)]]. Thus, the backbone PNA structure of Nielsen et al. is clearly suggested and motivated in Manoharan et al. Manoharan et al. is mostly directed to the preparation of amine terminated polymers, mostly oligonucleotides, wherein the amine is useful in linking to some other moiety. Such moieties are generically summarized in column 1, lines 25-48. These moieties are more specifically listed to include types such as given in column 15, lines 26-67, to include cell receptor binding molecules, alkylating agents, porphyrins, and crosslinkers. These moieties, linked to a terminal amine of PNAs suggest and these species of the instant invention. It is noted that several of the conjugate moieties listed in instant claim 1 are included.

Nielsen et al. describes a PNA with its backbone structure on page 1498, Figure 1 which is included as a specie in the PNA backbones of the instant claims.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the instant invention because Manoharan et al. suggests and motivates several species therein including a PNA with a cell receptor binding molecule etc. attached on the amino terminus as is also given in the instant claims.

The above applied Manoharan et al. reference has a common inventor and assignee with the instant invention. Based upon the earlier effective U.S. filing date of the reference, it

constitutes prior art under 35 U.S.C. 102(e). The above rejection under 35 U.S.C. 103(a) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another", or by a showing of a date of invention for the instant application of any unclaimed subject matter prior to the effective U.S. filing date of the reference under 37 CFR 1.131. This paragraph also applies to that portion of the below rejection based on the combination of references that includes Manoharan et al.

Claims 1, 5, 8-10, 12, 13, 15, 18-20, 22-24, 30-33, 37, 40, 42, 43, 45, and 50 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Thomson et al. (WO 93/12129); recently cited of record; or Manoharan et al. (P/N 5,834,607), taken in view of Nielsen et al. [Science 254:1497(1991); already of record]; either set of references taken in view of Ward et al. (P/n 4,711,955).

The descriptions of either of Manoharan et al. in view of Nielsen et al. or Thomson et al. have been summarized above regarding suggesting and motivating certain species of the instant invention but lack conjugate practice involving the nucleobases of the PNA polymers of the invention.

Ward et al. describes the chemistry and hybridizability in hybridization assays of nucleobase labeled nucleic acids. PNAs are described either in Manoharan et al., Nielsen et al., or

Thomson et al. as being substitute polymers for nucleic acid hybridization assays. Presumably, the hydrogen bonding that mediates PNA and nucleic acid polymer hybridization in such assays is identical. Thus, an improved labeling method as given in Ward et al. is not only expected to be functional regarding nucleobase labeled PNAs but is motivated by the improvement described in Ward et al. wherein other labeling methods are replaced by non-radioactive methods of labeling nucleobases. Such labels are attached optionally via various linkers to nucleobases as would also be expected to be doable for PNA assay polymers.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the instant invention because either Manoharan et al. in view of Nielsen et al. or Thomson et al. suggests and motivates several PNA species polymer species for various uses and Ward et al. adds the improvement of nucleobase labeling for detection assays thus resulting in the instant claim species directed to nucleobase practice with reporter molecules or enzymes attached via these options as described in Ward et al. Ward et al. describes various detection modes including enzyme containing in columns 23-24.

Claims 39, 41, 44, and 46 are allowed.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703) 308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

August 23, 1999



ARDIN H. MARSCHEL
PRIMARY EXAMINER